DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
7200 Lake Ellenor Drive
Orlando, FL 32809

12/1/97

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CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER

FLA-98-06

November 14, 1997

Mr. Steven G. Anderson
President and CEO
CryoLife Inc.
1655 Roberts Boulevard, N.W.
Kennesaw, Georgia 30144

Dear Mr. Anderson:

We are writing to you because on October 27-31, 1997, FDA Investigator Ronald T. Weber collected information that revealed serious regulatory problems involving the carotid shunts, which are manufactured and distributed by your firm, Ideas for Medicine.

Under the Federal Food, Drug, and Cosmetic Act (the Act), these products are considered to be a medical devices because they are used to treat medical conditions or to affect the structure or function of the body. The law requires that manufacturers of medical devices conform with the Quality System Regulation (QSR) as specified in Title 21, Code of Federal Regulations (CFR), Part 820.

The inspection revealed that the devices are adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for the manufacture, processing, packing, storage or distribution are not in conformance with the Quality System Regulation. These violations include, but are not limited to the following:

- Failure to implement corrective and preventive action for the recurrence of nonconforming product in the manufacture of carotid shunts, e.g., a significant number of complaints received by IFM involve carotid shunts which exhibit balloon failures or leakage, and IFM has failed to verify or determine the causes of these product nonconformities or initiate actions required to make the necessary corrections.

- Failure to validate significant manufacturing processes and quality assurance tests, e.g., there are no records documenting that validation has been conducted for

carotid shunts including latex formulation, latex balloon manufacturing including the joining of side arms to the dual lumen, and the process qualification conducted in February 1997 for safety balloon enlargement failed specifications.

- Failure to document, review, implement and validate changes to components, finished devices, labeling, packaging, or manufacturing process specifications, e.g., there are no control records documenting changes made to the punch process for the T-ports and the reduction of the ID of the latex balloons assuring the changes were reviewed and approved by management; there are no records documenting the verification or validation for drying time required after the T-joint is added, and for process changes made for the use of [redacted] to eliminate leaks at the T-joint and balloon inflation arms.

- Failure to establish and implement an adequate failure investigation program for handling complaints, e.g., 12 complaints concerning carotid shunt balloons were received in 1997 but not confirmed.

- Failure to have and follow procedures that document the acceptance of incoming components, e.g., components are accepted based on a certificate with no physical, material or functional testing verifying components meet specifications other than basic dimensions.

- Failure to establish adequate procedures for identifying and conducting training for all production and operational personnel, e.g., documentation does not adequately reflect required training, training received and those responsible for conducting training.

The carotid shunts may also be misbranded within the meaning of section 502(t) of the Act because the results of some investigations or additional information concerning MDR reportable events was not furnished to the Agency.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483, Inspectional Observations, issued to William F. Wright, General Manager, at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and

quality assurance systems (copy enclosed). You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

This also acknowledges your firm's letter dated November 7, 1997 signed by William F. Wright responding to the FDA 483. The response was reviewed and appears to be adequate to effect corrections to the listed observations. The response will be made part of your firm's file maintained in the Florida District.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for devices to which the GMP deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates for Products for Export will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office in writing within 15 working days of receipt of this letter, of any additional specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. Your firm's response states that most of the corrections have already been completed or will be completed by the end of December 1997. If for any reason there are delays in the time your promised corrections will be completed, please advise this office in writing when you anticipate all of your corrections will be completed. This will assist us in scheduling a reinspection of your firm to verify your promised corrective actions.

Your response should be directed to Timothy J. Couzins, Compliance Officer, Food and Drug Administration, 7200 Lake Ellenor Drive, #120. Orlando, Florida 32809, or call (407) 648-6823, ext. #264.

Sincerely yours,

Michael A. Chappell
Acting District Director
Florida District

Enclosure